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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,930	05/30/2001	Blake J. Roessler	UM-06192	7740

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

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DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application N .

09/867,930

Applicant(s)

ROESSLER ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

1. Claims 1-13 are currently under examination.

#### *Response to Arguments*

2. Applicant's arguments with respect to claims 1-13 have been considered but are moot in view of the new ground(s) of rejection made in response to Applicant's amendment.

#### *Claim Rejections - 35 USC § 102*

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 4 and 6-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kunz et al.

Claims 1, 4, 6-13 are drawn to (1) a composition comprising a nanoemulsion formulation, wherein the nanoemulsion formulation comprises an aqueous component, an oil component, and a surfactant mixture component, wherein said surfactant mixture component comprises a low HLB value surfactant and a high HLB value surfactant and wherein said nanoemulsion formulation comprises a biological agent, said biological agent comprising a nucleic acid; (4) wherein the low HLB surfactant has an HLB between approximately 3.3 and 5.3 and the high HLB value surfactant has an HLB value between approximately 14.0 and 16.0; 6) wherein said nanoemulsion does not contain short-chain alcohols; (7) wherein said low HLB surfactant is present in a greater amount than said high HLB value surfactant; (8) wherein said surfactant

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mixture component comprises a low HLB value non-ionic surfactant and a high HLB value non-ionic surfactant.

Claims 9-10 are drawn to (9) a composition comprising a nanoemulsion formulation comprising nucleic acid, that permits a skin permeation rate of at least 0.447% per hour for a biological agent in said nanoemulsion formulation; (10) wherein said skin permeation rate is selected from at least 0.519% per hour, at least 0.615% per hour, and at least 0.823% per hour.

Claims 11-12 are drawn to (11) a composition comprising a nanoemulsion formulation comprising an expression vector, wherein said nanoemulsion formulation permits the expression vector to express a recombinant peptide at a mean level of at least 57.0 pg/cm<sup>2</sup> in cells; (12) wherein said recombinant peptide is expressed at a mean level selected from at least 100.0 pg/cm<sup>2</sup>, at least 285.0 pg/cm<sup>2</sup>, and at least 376.0 pg/cm<sup>2</sup>.

Claim 13 is drawn to a composition comprising a nanoemulsion formulation comprising a nucleic acid expression vector, which permits an expression vector to express RNA transcripts at a level of at least  $5.0 \times 10^4$  transcripts/cm<sup>2</sup> in cells.

On page 13, lines 14-16, of the specification as filed, Applicants define the term “nanoemulsion formulation” as referring to “a composition comprising an aqueous component, an oil component, and a surfactant mixture component.” Therefore any composition that comprises these elements will be interpreted as reading on a “nanoemulsion formulation.”

Kunz et al. disclose delivery compositions that include a bioactive agent, an oil component, an oil-immiscible component, and a non-cationic surface-active agent (see page 27, lines 3-7). These compositions may be in the form of a microemulsion (page 28, lines 14-15). The compositions of Kunz et al. may comprise wherein the surface-active agent may encompass

a first and a second surface-active agent of non-identical structures. In these systems, the first surface-active agent may have an HLB of 8 or less and the second surface-active agent may have an HLB of 10 or greater. (It is noted that the limitation "between approximately 3.3 and 5.3" recited in claim 4 is broad enough to encompass an HLB value of 8 or less as disclosed in Kunz et al. due to the term "approximately".) In addition, both the first and second surface-active agents may be non-ionic (see page 27, lines 14-29). The bioactive agents of Kunz et al. are nucleic acid, preferably nucleic acid useful in gene therapy (see page 6, lines 9-10). The bioactive agents of Kunz et al. may also comprise expression vectors, i.e. plasmids, that may be used to express genes in host cells, see page 21, lines 5-19.

Kunz et al. state that the disclosed microemulsions may require a second interfacial film stabilizing agent or co-surfactant, the co-surfactant may be a second surfactant of differing HLB than the primary surfactant, short-chain alcohol or ester, carboxylic acid, organic amine, etc. To the extent that the co-surfactant may be a short-chain ester, carboxylic acid, organic amine, etc., the compositions of Kunz et al. encompass wherein the co-surfactant is not a short-chain alcohol (see bridging paragraph, pages 29-30).

Moreover, since Kunz et al. discloses a nanoemulsion formulation according to the present invention, absent evidence to the contrary, the nanoemulsion formulations of Kunz et al. would function to permit a skin permeation rate of at least 0.447% per hour for a biological agent in said nanoemulsion formulation; wherein said skin permeation rate is selected from at least 0.519% per hour, at least 0.615% per hour, and at least 0.823% per hour; permit an expression vector to express a recombinant peptide at a mean level of at least 57.0 pg/cm<sup>2</sup> in cells; wherein said recombinant peptide is expressed at a mean level selected from at least 100.0 pg/cm<sup>2</sup>, at

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least 285.0 pg/cm<sup>2</sup>, and at least 376.0 pg/cm<sup>2</sup>, and furthermore to permit an expression vector to express RNA transcripts at a level of at least  $5.0 \times 10^4$  transcripts/cm<sup>2</sup> in cells.

Kunz et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kunz et al. as evidenced by Dederen et al.

Claims 2-3 are drawn to the composition of claims 1, wherein the ratio of said low HLB value surfactant to said high HLB value surfactant is at least 2:1 or at least 3:1.

Discussion of Kunz et al. as set forth in the above rejection is incorporated here. However, Kunz et al. does not specifically teach formulations comprising wherein the ration of low HLB value surfactant to said high HLB value surfactant is at least 2:1 or at least 3:1.

Kunz et al. does teach compositions comprising both a high HLB surfactant and a low HLB surfactant, wherein that high HLB refers to HLB values of 10 or greater, and low HLB values refers to values of 8 or less. However, although Kunz et al. does not specifically recite wherein the ratio of low HLB value surfactant to said high HLB value surfactant is at least 2:1 or at least 3:1, the ratios of low HLB surfactants to high HLB surfactants recited in the instant

claims fall within the scope of the invention of Kunz et al., wherein nanoemulsion formulations comprising an excess in low HLB surfactants are preferred.

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Kunz et al. by optimizing the ratio of low HLB surfactant to high HLB surfactant to produce the compositions of the present invention. One of ordinary skill in the art would have been motivated to optimize this ratio since the ratio of low HLB to high HLB is disclosed in the prior art as being critical for determining the stability of an emulsion, see Dederen et al., paragraph [0035]. Moreover, “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), MPEP § 2144.05.

Therefore, the invention as a whole is *prima facie* obvious over Kunz et al. as evidenced by Dederin et al.

### ***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 9:00AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps-Ford, Ph.D.  
Examiner  
Art Unit 1635

JLE  
July 11, 2003

  
KAREN LACOURCIERE  
PATENT EXAMINER